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10/502,279	07/23/2004	Hideki Endoh	Q82704	2122

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SUGHRUE MION, PLLC
2100 PENNSYLVANIA AVENUE, N.W.
SUITE 800
WASHINGTON, DC 20037

EXAMINER	
STEELE, AMBER D	
ART UNIT	**PAPER NUMBER**
1639	

DATE MAILED: 08/01/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/502,279	ENDOH ET AL.	
	Examiner	Art Unit	
	Amber D. Steele	1639	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *16 May 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-19* is/are pending in the application.

4a) Of the above claim(s) *1-16 and 19* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *17 and 18* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *26 October 2004* is/are: a)☐ accepted or b)☒ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of the Claims

1. Claims 1-19 are currently pending.

Claims 17-18 are currently under consideration.

Election/Restrictions

2. Applicant's election without traverse of Group XII (claims 17-18) in the reply filed on May 16, 2006 is acknowledged.

3. Claims 1-16 and 19 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected inventions, there being no allowable generic or linking claim. Election was made **without** traverse in the reply filed on May 16, 2006.

Priority

4. Receipt is acknowledged of papers submitted under 35 U.S.C. 119(a)-(d), which papers have been placed of record in the file for JP 2002-13721 and JP 2002-257703.

Information Disclosure Statement

5. The listing of references in the Search Report is not considered to be an information disclosure statement (IDS) complying with 37 CFR 1.98. 37 CFR 1.98(a)(2) requires a legible copy of: (1) each foreign patent; (2) each publication or that portion which caused it to be listed; (3) for each cited pending U.S. application, the application specification including claims, and

any drawing of the application, or that portion of the application which caused it to be listed including any claims directed to that portion, unless the cited pending U.S. application is stored in the Image File Wrapper (IFW) system; and (4) all other information, or that portion which caused it to be listed. In addition, each IDS must include a list of all patents, publications, applications, or other information submitted for consideration by the Office (see 37 CFR 1.98(a)(1) and (b)), and MPEP § 609.04(a), subsection I. states, "the list ... must be submitted on a separate paper." Therefore, the references cited in the Search Report have not been considered. Applicant is advised that the date of submission of any item of information or any missing element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the IDS, including all "statement" requirements of 37 CFR 1.97(e). See MPEP § 609.05(a). Therefore, the search reports listed in IDS have been considered but the individual references have not necessarily been considered unless a copy of the reference was provided.

6. The information disclosure statement filed October 26, 2004 fails to comply with the provisions of 37 CFR 1.97, 1.98 and MPEP § 609 because U.S. Patent 3,365,3651 does not exist. In addition, for application WO 97/31907 only the search report has been considered and for application JP 2001-340080 only pages 6-7 have been considered. The IDS has been placed in the application file, but the information referred to therein that has been crossed out or with a note has either not been considered as to the merits or only the portion recited in the note has been considered. Applicant is advised that the date of any re-submission of any item of information contained in this information disclosure statement or the submission of any missing

element(s) will be the date of submission for purposes of determining compliance with the requirements based on the time of filing the statement, including all certification requirements for statements under 37 CFR 1.97(e). See MPEP § 609.05(a).

Drawings

7. The drawings are objected to as failing to comply with 37 CFR 1.84(p)(5) because they include the following reference character(s) not mentioned in the description: While Figures 1, and 6 are described in the specification, Figures 1A, 1B, 1C, 6A, and 6B are not described. Corrected drawing sheets in compliance with 37 CFR 1.121(d), or **amendment to the specification to add the reference character(s) in the description** in compliance with 37 CFR 1.121(b) are required in reply to the Office action to avoid abandonment of the application. Any amended replacement drawing sheet should include all of the figures appearing on the immediate prior version of the sheet, even if only one figure is being amended. Each drawing sheet submitted after the filing date of an application must be labeled in the top margin as either "Replacement Sheet" or "New Sheet" pursuant to 37 CFR 1.121(d). If the changes are not accepted by the examiner, the applicant will be notified and informed of any required corrective action in the next Office action. The objection to the drawings will not be held in abeyance.

Specification

8. The abstract of the disclosure is objected to because it contains more than 150 words. (See MPEP § 608.01, Abstract of the Disclosure: A brief narrative of the disclosure as a whole in a single paragraph of 150 words or less commencing on a separate sheet following the

claims).

Applicant is reminded of the proper language and format for an abstract of the disclosure. The abstract should be in narrative form and generally limited to a single paragraph on a separate sheet within the range of 50 to 150 words. It is important that the abstract not exceed 150 words in length since the space provided for the abstract on the computer tape used by the printer is limited.

9. The specification has not been checked to the extent necessary to determine the presence of all possible minor errors. Applicant's cooperation is requested in correcting any errors of which applicant may become aware in the specification.

Claim Objections

10. Claims 17-18 are objected to because of the following informalities: The terms ameliorating and represented and the phrase transcription promoter activity are objected to.

A. The term ameliorating is defined as "to improve, to make or become better". However, the use of the term ameliorating pertaining to insulin resistance is somewhat ambiguous. For example, does ameliorating insulin resisitance mean that the insulin resistance is prevented, cured, or treated?

B. The term represented is ambiguous in the present context. For example, does a nucleic acid sequence that is represented by SEQ ID NO: 26 require a certain homology to SEQ ID NO: 26? Would a nucleic acid sequence from the same family of sequences represent SEQ ID NO: 26?

C. The phrase transcription promoter activity is ambiguous in the present context. For example, does SEQ ID NO: 26 have promoter activity, does SEQ ID NO: 26 alter promoter activity, or is SEQ ID NO: 26 controlled by a promoter region? Appropriate correction is required.

Claim Rejections - 35 USC § 112

11. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

12. Claims 17-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. Applicant is directed to the Guidelines for the Examination of Patent Applications under the 35 USC 112, first paragraph "Written Description" requirement, Federal Register, Vol. 66, No. 4 pages 1099-1111, Friday January 5, 2001. This is a **written description** rejection.

Claim 17 is drawn to a method for screening a drug ameliorating insulin resistance comprising (i) contacting a test substance with a cell transformed with a reporter gene fused to SEQ ID NO: 26 or a sequence represented by SEQ ID NO: 26 wherein 1-10 bases are deleted, substituted, and/or inserted and has transcription promoter activity and (ii) analyzing the change of the activity for transcriptional induction due to the test substance using the expression of a reporter gene. Although addressing a specific sequence with "transcription promoter activity" of

SEQ ID NO: 26, the method can also utilize any "nucleotide sequence represented by SEQ ID NO: 26 wherein 1-10 bases are deleted, substituted, and/or inserted and also having transcription promoter activity" wherein the deletions, substitutions, and insertions are not defined. In addition, the specification states that the promoter sequence for FLJ13111 is unknown and that SEQ ID NO: 26 contains part of the **coding** sequence for FLJ13111 gene at the 3' terminus, but does not provide definitive evidence that SEQ ID NO: 26 contains the promoter region responsible for transcription of the FLJ13111 gene (please refer to pages 100-101). The resulting data (Figure 9; Example 14) show that SEQ ID NO: 26 induces a very low level of luciferase activity which is more in line with the amount of activity observed with GAL4-PPARγ (e.g. a transcription factor; please refer to Figure 7) than to the amount expected of a transcription promoter that should cause a significant increase in luciferase expression. Additionally, a control with a known promoter region linked to luciferase was not shown therefore, the level of luciferase activity under normal promoter activity is not known. Furthermore, the Promega website provides information on the expected levels of luciferase activity utilizing the pGL3 vector which levels are far higher than the present data show (e.g. Promega date shows luciferase activity of 1,350 relative light units while the current data shows luciferase activity of 1.5-2.5 relative units; luciferase relative light units below 50 correlate to background activity; please refer to Figure 9 and Promega technical manual No. 033 for pGL3 Luciferase reporter vectors figures 6-7 available via the Promega website). Moreover, the claim encompasses any test substance/drug, any transcription factor or upstream signaling molecules that affect transcription factors, and any reporter gene that are known or unknown. Accordingly, the claims encompass a vast screening method of all factors that could alter any transcription factor or signaling molecule

(or any other factor) that potentially alters the activity of SEQ ID NO: 26 or (e.g. various deletions, substitutions, or insertions) SEQ ID NO: 26 variants. Intended use as a screen for a drug ameliorating insulin resistance is broad due to the ambiguous nature of the term "ameliorate" (e.g. improve, make or become better comprising any change including non-significant changes). Accordingly, the claim scope is unduly broad with respect to the encompassed screening method for drugs that ameliorate insulin resistance.

The specification teaches five types of thiazolidine derivatives (e.g. test substance/drug) including GW7282, Gl-262570, GL-100085, rosiglitazone, and pioglitazone wherein rosiglitazone and pioglitazone are commercially available drugs for treating Type II diabetes (please refer to pages 24 and 58-61; Table 1; Figures 7 and 11). In addition, the specification teaches the ability of SEQ ID NO: 26 to alter PPARγ and GAL4 (e.g. transcription factors; construct is a PPARγ and GAL4 chimera) activity in the presence of rosiglitazone or pioglitazone (e.g. pioglitazone affect is not significant) only but does not suggest that SEQ ID NO: 26 would have a similar effect on every known or potential transcription factor or other transcription factor chimeras (please refer to Examples 11-12; Figures 7 and 11). Furthermore, the specification teaches three reporter genes CAT, LUC, and GFP (please refer to pages 38-39). Therefore, one skilled in the relevant art would not reasonably conclude that the Applicants had possession of the invention as claimed.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was *in possession of the invention.* The invention is, for purposes of the 'written description' inquiry, *whatever is now claimed.*" (See page 1117.) The specification does not "clearly allow persons

of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See page 1116.).

With the exception of Examples 12 and 14 and Figures 7, 9, and 11 showing rosiglitazone and pioglitazone (although pioglitazone results are not significant) alter PPARγ activity via SEQ ID NO: 26 as disclosed by the specification, the skilled artisan cannot envision the method of claim 17. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016. In Fiddes v. Baird, 30 USPQ2d 1481, 1483, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class wherein the specification provided only the bovine sequence.

13. Claims 17-18 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the enablement requirement. The claim(s) contains subject matter which was not described in the specification in such a way as to enable one skilled in the art to which it pertains, or with which it is most nearly connected, to make and/or use the invention. This is an **enablement** rejection.

Claims 17-18 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for a method of screening thiazolidinedione derivatives rosiglitazone and pioglitazone (e.g. commercially available treatments for Type II diabetes) for alterations in PPARγ/GAL4 chimera transcription factor activity via SEQ ID NO: 26. The specification does

not enable a person skilled in the art to make and use the invention commensurate in scope with the claim.

There are many factors to consider when determining whether there is sufficient evidence to support a determination that a disclosure does not satisfy the enablement requirement and whether any experimentation is "undue". These factors include, but are not limited to:

1. The breadth of the claims;
2. The nature of the invention;
3. The state of the prior art;
4. The level of skill in the art;
5. The level of predictability in the art;
6. The amount of direction provided by the inventor;
7. The presence or absence of working examples;
8. The quantity of experimentation necessary needed to make or use the invention based on the disclosure.

See *In re Wands* USPQ 2d 1400 (CAFC 1988):

The breadth of the claims and the nature of the invention:

Although addressing a specific sequence with "transcription promoter activity" of SEQ ID NO: 26, the method can also utilize any "nucleotide sequence represented by SEQ ID NO: 26 wherein 1-10 bases are deleted, substituted, and/or inserted and also having transcription promoter activity" wherein the deletions, substitutions, and insertions are not defined. In addition, the claim encompasses any test substance/drug, any transcription factor or upstream signaling molecules that affect transcription factors, and any reporter gene that are known or

unknown. Accordingly, the claims encompass a vast screening method of all factors that could alter any transcription factor or signaling molecule (or any other factor) that potentially alters the activity of SEQ ID NO: 26 or (e.g. various deletions, substitutions, or insertions) SEQ ID NO: 26 variants. Intended use as a screen for a drug ameliorating insulin resistance is broad due to the indefiniteness of "ameliorate" (e.g. improve, make or become better comprising any change including non-significant changes). Accordingly, the claim scope is unduly broad with respect to the encompassed screening method for drugs that ameliorate insulin resistance.

The state of the prior art and the level of predictability in the art:

Very little information is known about the function of CENP-T (e.g. FLJ13111, FLJ43376, C16orf56, centromere protein T; SEQ ID NO: 26). The present specification states that "no information indicating the molecular function of FLJ13111 based on the amino acid sequence and the structure except that the presence of a nucleus targeting sequence and the presence of a site to be possibly glycosylated within the molecule" is known (please refer to page 8, lines 3-9 of the present specification). In addition, Foltz et al. teach that CENP-T (e.g. FLJ13111, FLJ43376, C16orf56, centromere protein T) associates with CENP-A nucleosomes and if suppressed by siRNA dramatically alters mitosis (*Nature Cell Biology*, 8(5): 458-469 and supplements 1-4, 2006; please refer to Tables 1 and S1; sections "Identification of the CENP-A NAC", "The CENP-A NAC complex recruits a set of CADs", "CENP-M, CENP-N, and CENP-T are required for proper assembly of the CENP-A NAC", "CENP-A NAC is required for proper mitotic progression"; "Discussion"; Figures 2-4, 6, S1, S3). The only known function of CENP-T is complexing with other CENP proteins to form the CENP-A NAC complex and the ability of

CENP-T to alter mitosis. It is not clear from the present specification how altered mitosis is related to insulin resistance.

In addition, the specification states that the promoter sequence for FLJ13111 is unknown and that SEQ ID NO: 26 contains part of the **coding** sequence for FLJ13111 gene at the 3' terminus, but does not provide definitive evidence that SEQ ID NO: 26 contains the promoter region responsible for transcription of the FLJ13111 gene (please refer to pages 100-101). The resulting data (Figure 9; Example 14) show that SEQ ID NO: 26 induces a very low level of luciferase activity which is more in line with the amount of activity observed with GAL4-PPARγ (e.g. a transcription factor; please refer to Figure 7) than to the amount expected of a transcription promoter that should cause a significant increase in luciferase expression. Additionally, a control with a known promoter region linked to luciferase was not shown therefore, the level of luciferase activity under normal promoter activity is not known. Furthermore, the Promega website provides information on the expected levels of luciferase activity utilizing the pGL3 vector which levels are far higher than the present data show (e.g. Promega date shows luciferase activity of 1,350 relative light units while the current data shows luciferase activity of 1.5-2.5 relative units; luciferase relative light units below 50 correlate to background activity; please refer to Figure 9 and Promega technical manual No. 033 for pGL3 Luciferase reporter vectors figures 6-7 available via the Promega website).

Simply because CENP-T expression is decreased in some diabetic mice (Figure 8; a significant decrease was observed between KKA diabetic mice and C57Bl mice however, normal mice m+/m+ had similar levels to both KKA and db/db diabetic mice), a definitive correlation between FLJ13111 and diabetes is not shown since other factors could be contributing to the

reduced level of FLJ13111 which are not related to diabetes. In addition, the statement in the specification that the reduction in FLJ13111 expression lecvel in the muscle triggers insulin resistance is completely unfounded (please refer to page 100; more definative experimentation would be required to conclude that a decrease in FLJ13111 alone causes diabetes). Furthermore, the elevated luciferase activity in the presence of FLJ13111, GAL4-PPARγ chimera, and rosiglitazone over GAL4-PPARγ chimera and rosiglitazone alone (Figure 7) does not provide adequate support that any drug or all drugs that would cause elevated luciferase activity in the presence of FLJ13111 or FLJ13111 promoter would also ameliorate insulin resistance. In fact, a known drug for treatment of Type II diabetes which is able to "ameliorate" insulin resistance (e.g. pioglitazone) did not have a significant response to FLJ13111 or significantly alter FLJ13111 "promoter" activity (e.g. luciferase activity of approximately 0.11 with GAL4-PPARγ and pioglitazone alone and approximately 0.14 with the addition of FLJ13111 is not a significant increase, see Figure 11; approximately 1.5 luciferase units for FLJ13111 "promoter" alone and approximately 2.5 luciferase units for pioglitazone and FLJ13111 "promoter" is not a significant increase, see Figure 9). The date shown utilizing two known drugs (e.g. rosiglitazone and pioglitazone) of the same class shown different results regarding FLJ13111 activity (e.g. rosiglitazone agonist function for PPARγ is elevated in the presence of FLJ13111 while pioglitazone agonist function for PPARγ is not significantly altered by FLJ13111) therefore definitive statements about the correlation between FLJ13111 and insulin resistance are not fully supported.

The level of skill in the art:

The level of skill would be high, most likely at the Ph.D. level.

The amount of direction provided by the inventor and the existence of working examples:

While examples and data are provided utilizing SEQ ID NO: 26 (e.g. FLJ13111, CENP-T), GAL4-PPARγ (e.g. transcription factor chimera), luciferase (e.g. reporter) and pioglitazone and rosiglitazone (e.g. drugs; Figures 7, 9, and 11), the examples do not conclusively show that any drug that "ameliorates" insulin resistance will significantly alter transcription promoter activity of SEQ ID NO: 26. In fact, a known drug for treatment of Type II diabetes which is able to "ameliorate" insulin resistance (e.g. pioglitazone) did not have a significant response to FLJ13111 (e.g. luciferase activity of approximately 0.11 with GAL4-PPARγ and pioglitazone alone and approximately 0.14 with the addition of FLJ13111 is not a significant increase, see Figure 11; approximately 1.5 luciferase units for FLJ13111 "promoter" alone and approximately 2.5 luciferase units for pioglitazone and FLJ13111 "promoter" is not a significant increase, see Figure 9). Furthermore, the inventors only utilize SEQ ID NO: 26, luciferase, and thiazolidinedione derivatives in the screening assay while the invention claims that any drug can be screened, and claims any reporter gene can be utilized. The method as presently claimed suggests that the drug or test substance being screened would have to directly affect SEQ ID NO: 26 without the presence of other factors (e.g. GAL4-PPARγ chimera). The only example provided (e.g. Figure 9 and Example 14) that read on the method do not clearly state how the method was performed. For example the Promega pGL3 luciferase reporter vectors were utilized but these vectors can be utilized for determining both cis-acting (e.g. promoters and enhancers) and trans-acting (e.g. DNA binding factors) affects and the specification does not clearly state which of the vectors was utilized. Therefore, what could be perceived as promoter activity may

actually be DNA binding activity. Considering the known activity of FLJ13111 as a centromere binding protein important in mitosis, the DNA binding activity of FLJ13111 would be expected.

The quantity of experimentation needed to make or use the invention based on the content of the disclosure:

In light of the unpredictability surrounding the claimed subject matter, the undue breadth of the claimed invention's intended use, and the lack of adequate guidance to practice the presently claimed invention would be unable to do so without engaging in undue experimentation. As a result of the broad and unpredictable nature of the invention and the lack of specific guidance from the specification, the Examiner contends that the quantity of experimentation needed to make and or use the invention would be great. Note that there must be sufficient disclosure, either through illustrative examples or terminology, to teach those of ordinary skill how to make and use the invention as broadly as it is claimed. *In re Vaeck*, 947 F.2d 488, 496 & n.23, 20 USPQ2d 1438, 1445 * n.23 (Fed. Cir. 19991). In this case, Applicants have not provided sufficient working examples that would teach this enormous genus that falls within a highly unpredictable art area. Therefore, it is deemed that further research of an unpredictable nature would be necessary to make or use the invention as claimed. Thus, due to the inadequacies of the instant disclosure one of ordinary skill would not have a reasonable expectation of success and the practice of the full scope of the invention would require undue experimentation.

Therefore based on the evidences as a whole regarding each of the above factors (e.g. factors 1-8), the specification, at the time the application was filed, does not satisfy the enablement requirement for the instant claimed method of screening a drug ameliorating insulin

resistance comprising: i. contacting a test substance with a cell transformed with a reporter gene fused to SEQ ID NO: 26 or a nucleotide sequence represented by SEQ ID NO: 26 wherein 1-10 bases are deleted, substituted, or inserted and having transcriptional promoter activity, and ii. analyzing the change of the activity for transcriptional induction due to the test substance using the expression of a reporter gene.

Claim Interpretation

14. The presently claimed invention is directed to:

A method for screening a drug ameliorating insulin resistance comprising:

i. contacting a test substance with a cell transformed with a reporter gene fused to SEQ ID NO: 26 or a nucleotide sequence represented by SEQ ID NO: 26 wherein 1-10 bases are deleted, substituted, or inserted and having transcriptional promoter activity, and

ii. analyzing the change of the activity for transcriptional induction due to the test substance using the expression of a reporter gene.

Claim Rejections - 35 USC § 103

15. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

16. Claims 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Doebber et al. U.S. Patent 5,847, 008 issued December 8, 1998 and Shimkets and Leach WO 00/58473 published October 5, 2000.

For present claim 17, Doebber et al. teaches methods of screening antidiabetic (e.g. Type II diabetes) compounds for alteration of transcriptional elements related to PPARγ (please refer to abstract; columns 1-2). In addition, Doebber et al. teach method steps of contacting cells transfected with transcription promoter and reporter with test compounds and analyzing the change in transcription promoter activity and utilizing PPAR-responsive reporter construct (e.g. pPPAR-luc; please refer to columns 20-24).

For present claim 18, Doebber et al. teach using luciferase as the reporter gene (please refer to column 23, lines 40-62).

However, Doebber et al. do not teach SEQ ID NO: 26.

Shimkets and Leach teach SEQ ID NO: 26 (e.g. CENP-T, C16orf56, FLJ43376, or FLJ13111) and the use of ORFX (e.g. SEQ ID NO: 26) in screening assays including the two-hybrid assay for testing compounds including drugs. In addition, Shimkets and Leach teach that the ORFXs may be important in various diseases including diabetes. See entire document particularly pages 49-59 and sequence listing.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the screening assays of Doebber et al. with the sequences taught by Shimkets and Leach.

One having ordinary skill in the art would have been motivated to do this because Shimkets and Leach teach that the ORFXs may be important is various diseases including

diabetes (please refer to pages 49-59). In addition, the expansion of the screening method taught by Taniguchi and Mizukami to include new sequences with unknown properties would be a design choice based on the desire to expand the screening method.

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the screening assays of Doebber et al. with the sequences taught by Shimkets and Leach because the Examples taught by Doebber et al. making various compounds with antidiabetic properties.

Therefore, the modification of the screening assays of Doebber et al. with the sequences taught by Shimkets and Leach render the instant claims *prima facie* obvious.

17. Claims 17-18 are rejected under 35 U.S.C. 103(a) as being unpatentable over Taniguchi and Mizukami EP 1 057 896 A1 published December 6, 2000 (published March 3, 1999 as WO 99/10532) and Shimkets and Leach WO 00/58473 published October 5, 2000.

For present claim 17, Taniguchi and Mizukami teach methods of screening agonists or antagonists which can be used as treatments for diabetes for PPARγ via contacting a cell and a test substance and analyzing the reporter gene level. In addition, Taniguchi and Mizukami teach utilizing two-hybrid systems, reporter genes, GAL4, PPARγ, in the methods. Please refer to abstract; paragraphs 5-11 and 24-50; Examples.

For present claim 18, Taniguchi and Mizukami teach luciferase as the reporter gene (please refer to paragraph 39).

However, Taniguchi and Mizukami do not teach SEQ ID NO: 26.

Shimkets and Leach teach SEQ ID NO: 26 (e.g. CENP-T, C16orf56, FLJ43376, or FLJ13111) and the use of ORFX (e.g. SEQ ID NO: 26) in screening assays including the two-hybrid assay for testing compounds including drugs. In addition, Shimkets and Leach teach that the ORFXs may be important in various diseases including diabetes. See entire document particularly pages 49-59 and sequence listing.

It would have been obvious to a person of ordinary skill in the art at the time the invention was made to modify the screening assay of Taniguchi and Mizukami with the sequences of Shimkets and Leach.

One having ordinary skill in the art would have been motivated to do this because Shimkets and Leach teach that the ORFXs may be important is various diseases including diabetes (please refer to pages 49-59). In addition, the expansion of the screening method taught by Taniguchi and Mizukami to include new sequences with unknown properties would be a design choice based on the desire to expand the screening method.

One of ordinary skill in the art would have had a reasonable expectation of success in the modification of the screening assay of Taniguchi and Mizukami with the sequences of Shimkets and Leach because of the Examples taught by Taniguchi and Mizukami showing that the screening method provides agonists and antagonists for the treatment of diabetes.

Therefore, the modification of the screening assay of Taniguchi and Mizukami with the sequences of Shimkets and Leach render the instant claims *prima facie* obvious.

Future Communications

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Amber D. Steele whose telephone number is 571-272-5538. The examiner can normally be reached on Monday through Friday 9:00AM-5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Peter Paras can be reached on 571-272-4517. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

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PETER PARAS, JR.
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600